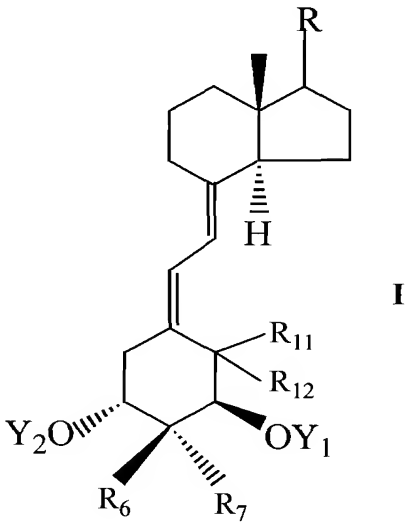
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method of increasing rate of skeletal repair in a mammal having a bone implant or bone transplant by stimulating osteoblast-mediated growth of new bone at the site of the transplant or implant, ~~in a mammal~~ comprising administering to ~~a mammal in need thereof~~ the mammal at the site of the implant or transplant, in an immobilized, slow release form, a therapeutically effective amount of a compound having the formula:



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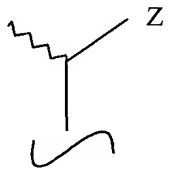
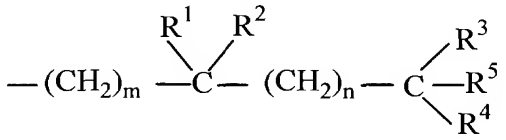
where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, where R_{11} and R_{12} are each hydrogen or taken together are a methylene group, where R_6 and R_7, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, fluoroalkyl, hydroxy and alkoxy, with the proviso that R_6 and R_7 cannot both be hydrogen, or R_6 and R_7 when taken together may represent the group $-(CH_2)_x-$

where X is an integer from 2 to 5, or R_6 and R_7 when taken together may represent the group $=CR_8R_9$ where R_8 and R_9, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, fluoroalkyl, hydroxy and alkoxy, or when taken together R_8 and R_9 may represent the group $-(CH_2)_x-$ where X is an integer from 2 to 5, and where the group R represents



where the stereochemical center (corresponding to C-20 in steroid numbering) may have the R or S configuration, (i.e. either the natural configuration about carbon 20 or the 20-epi configuration), and where Z is selected from Y, -OY, $-CH_2OY$,

-C≡CY and -CH=CHY, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:



where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and

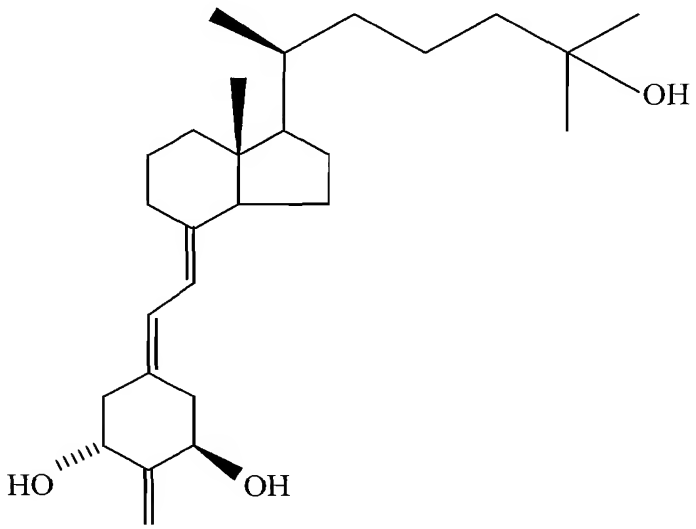
where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy, or C_{1-5} alkyl and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-(CH_2)_m-$, $-CR_1R_2-$ or $-(CH_2)_n-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

2.-7. (Cancelled)

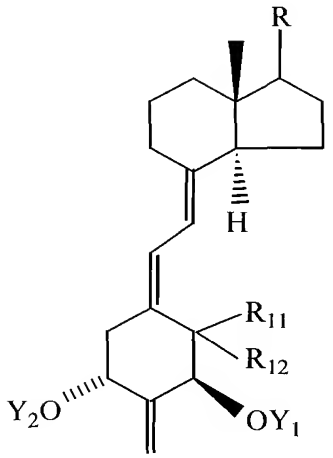
8. (Original) The method of claim 1 wherein the compound is administered in a dosage of from 0.01μg to 50μg per day.

9. (Original) The method of claim 1 wherein the mammal is a human.

10. (Original) The method of claim 1 wherein the compound administered is 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D_3 having the formula:



11. (Original) The method of claim 1 wherein the compound administered is an acylated derivative having the formula:



where Y^1 and Y^2 independently represent hydrogen or an acyl group, and with the proviso that R^5 is $-OY_3$ and Y_3 is selected from the group consisting of acyl or a hydrocarbyloxycarbonyl.

12. (Original) The method of claim 11 wherein the compound is a triacetate such that Y_1, Y_2 and Y_3 and each CH_3CO-.

13. (Original) The method of claim 11 wherein the compound as a trihexanoate such that Y_1, Y_2 and Y_3 are each $CH_3(CH_2)_4CO$-.

14. (Original) The method of claim 11 wherein the compound is a trinonanoate such that Y_1, Y_2 and Y_3 are each $CH_3(CH_2)_7CO$-.

15. (Original) The method of claim 11 wherein the compound is a 25-acetate such that Y_1 and Y_2 are both hydrogen and Y_3 is CH_3CO-.

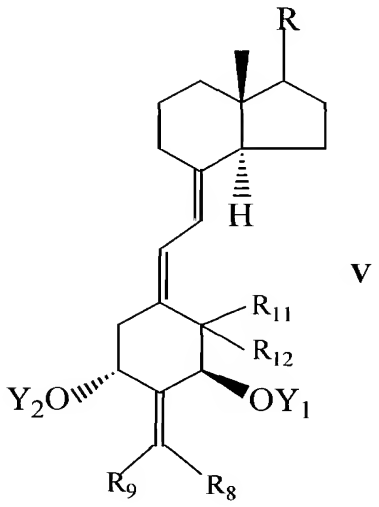
16. (Original) The method of claim 11 wherein the compound is 2-methylene-19-nor-1α,25$(OH)_2$-D_3-1,3,25-triacetate.

17. (Original) The method of claim 11 wherein the compound is 2-methylene-19-nor-1α,25(OH)$_2$-D$_3$-1,3,25-trihexanoate.

18. (Original) The method of claim 11 wherein the compound is 2-methylene-19-nor-1α,25(OH)$_2$-D$_3$-1,3,25-trinonanoate.

19. (Original) The method of claim 11 wherein the compound is 2-methylene-19-nor-1α,25(OH)$_2$-D$_3$-25-acetate.

20. (Original) The method of claim 1 wherein the compound administered is selected from the group consisting of:



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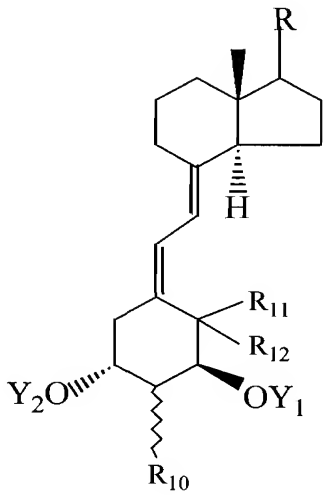
where Y_1, Y_2, R_{11}, R_{12} and R are as defined in claim 1 and R_8 and R_9, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or, when taken together represent the group -$(CH_2)_X$- where X is an integer from 2 to 5.

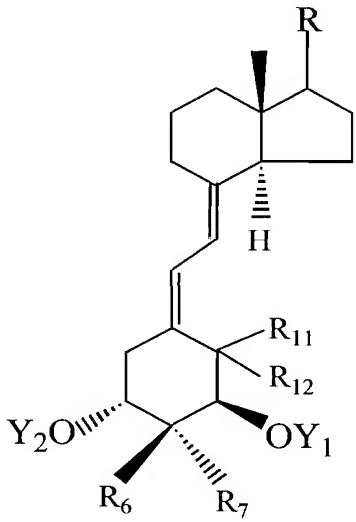
21. (Original) The method of claim 1 wherein the compound administered is selected from the group consisting of:



VI

where Y_1, Y_2, R_{11} and R_{12} and R are as defined in claim 1 and R_{10} is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl.

22. (Original) The method of claim 1 wherein the compound administered is selected from the group consisting of:

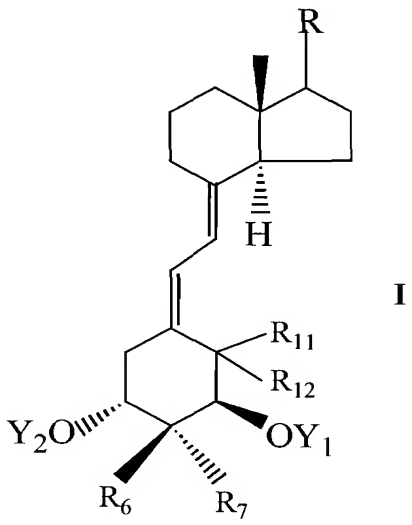


VII

where Y_1, Y_2, R_{11}, R_{12}, R_6, R_7 and R are as defined in claim 1 with the proviso that R^5 is -OY_3 and Y_3 is selected from the group consisting of an acyl or a hydrocarbyloxycarbonyl.

23.-28. (Cancelled)

29. (New) A method of increasing rate of skeletal repair in a mammal having a bone implant or bone transplant by stimulating osteoblast-mediated growth of new bone at the site of the transplant or implant, comprising administering to the mammal at the site of the implant or transplant, in an immobilized form, a therapeutically effective amount of a compound having the formula:



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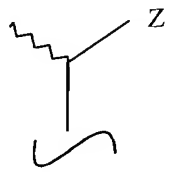
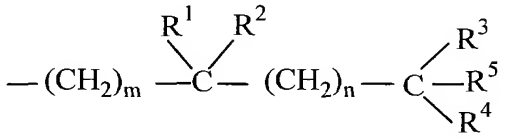
where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, where R_{11} and R_{12} are each hydrogen or taken together are a methylene group, where R_6 and R_7, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, fluoroalkyl, hydroxy and alkoxy, with the proviso that R_6 and R_7 cannot both be hydrogen, or R_6 and R_7 when taken together may represent the group $-(CH_2)_x-$ where X is an integer from 2 to 5, or R_6 and R_7 when taken together may represent the group $=CR_8R_9$ where R_8 and R_9, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, fluoroalkyl, hydroxy and

alkoxy, or when taken together R_8 and R_9 may represent the group $-(CH_2)_x-$ where X is an integer from 2 to 5, and where the group R represents



where the stereochemical center (corresponding to C-20 in steroid numbering) may have the R or S configuration, (i.e. either the natural configuration about carbon 20 or the 20-epi configuration), and where Z is selected from Y, -OY, $-CH_2OY$,

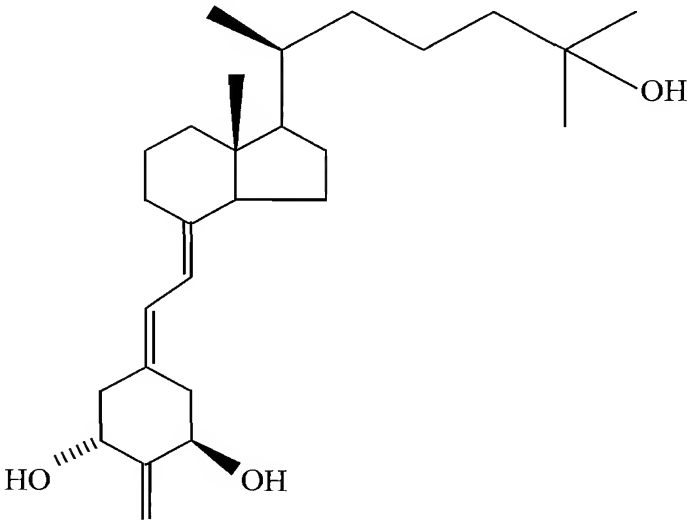
-C≡CY and -CH=CHY, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:



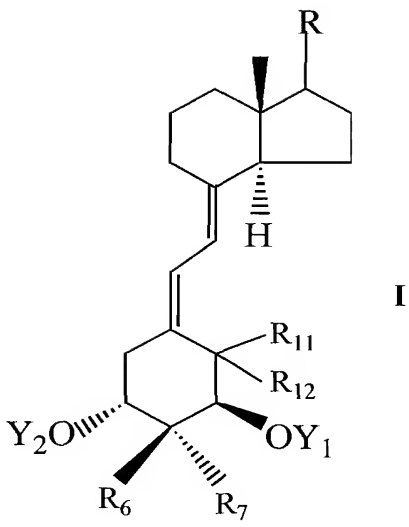
where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy,

or C_{1-5} alkyl and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-(CH_2)_m-$, $-CR_1R_2-$ or $-(CH_2)_n-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

30. (New) The method of claim 29 wherein the compound administered is 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D_3 having the formula:



31. (New) A method of increasing rate of skeletal repair in a mammal having a bone implant or bone transplant by stimulating osteoblast-mediated growth of new bone at the site of the transplant or implant, comprising administering to the mammal at the site of the implant or transplant, in slow release form, a therapeutically effective amount of a compound having the formula:



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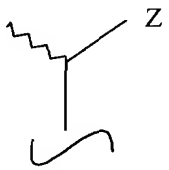
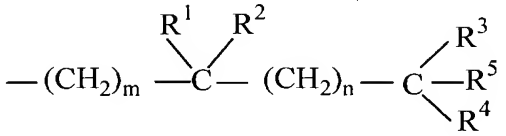
where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, where R_{11} and R_{12} are each hydrogen or taken together are a methylene group, where R_6 and R_7, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, fluoroalkyl, hydroxy and alkoxy, with the proviso that R_6 and R_7 cannot both be hydrogen, or R_6 and R_7 when taken together may represent the group $-(CH_2)_x-$ where X is an integer from 2 to 5, or R_6 and R_7 when taken together may represent the group $=CR_8R_9$ where R_8 and R_9, which may be the same or different, are each selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, fluoroalkyl, hydroxy and alkoxy, or when taken together R_8 and R_9 may represent the group $-(CH_2)_x-$ where X is an integer from 2 to 5, and where the group R represents



where the stereochemical center (corresponding to C-20 in steroid numbering) may have the R or S configuration, (i.e. either the natural configuration about carbon 20 or the 20-epi configuration), and where Z is selected from Y, -OY, $-CH_2OY$,

-C≡CY and -CH=CHY, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:



where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy, or C_{1-5} alkyl and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-(CH_2)_m-$, $-CR_1R_2-$ or $-(CH_2)_n-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

32. (New) The method of claim 31 wherein the compound administered is 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D_3 having the formula: